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EXAMINER	
SANDALS, WILLIAM O	

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/844,508	Wolffe et al.
Examiner	**Art Unit**
William Sandals	1636

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 11, 2003*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above, claim(s) *7, 9, 14-16, 34-42, 71, and 72* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6, 8, 10-13, 17-33, and 43-70* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Apr 11, 2003* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 1-72 are pending. Claims 7, 9, 14-16, 34-42 71 and 72 are withdrawn from examination as being drawn to a non-elected invention.

2. The provisional rejection of claims 1-72 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-42 and 44-73 of copending Application No. 10/084,826 is withdrawn in view of Applicant's cancellation of said copending claims.

3. The rejection of claims 1-6, 8, 10, 12, 13, 17-20, 43-47, 55-57, 59-62, 64-66 and 68-70 under 35 U.S.C. 102(e) as being anticipated by US 2002/0045158 A1 (Case) has been overcome by amendment.

4. The rejection of claims 1-6, 8, 12, 13, 17, 43-46, 55, 57, 59-61 and 64-70 under 35 U.S.C. 102(e) as being anticipated by US 2002/0188103 A1 (Bestor) has been overcome by amendment.

5. The rejection of claims 1-6, 8, 10, 12, 13, 17-33 and 43-70 under 35 U.S.C. 103(a) as being unpatentable over each of US 2002/0045158 A1 (Case) and US 2002/0188103 A1 (Bestor) in view of US 6,015,709 (Natesan) and US 6,153,383 (Verdine et al.) has been overcome by amendment.

6. Claims 1-6, 8, 10-13, 17-33 and 43-70 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 and 17-20 of copending Application No. 09/942,087.

7. Claims 1-6, 8, 10-13, 17-33 and 43-70 stand rejected under 35 U.S.C. 112, first paragraph

8. Claims 1-6, 8, 10-13, 17-33 and 43-70 stand rejected under 35 U.S.C. 112, second paragraph.

9. New grounds of rejection are presented below.

Drawings

10. The drawings as submitted on April 11, 2003, have been approved by the draftsman.

Response to Arguments

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-6, 8, 10-13, 17-33 and 43-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 and 17-20 of copending Application No. 09/942,087. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending Application No. 09/942,087 are drawn to a method of modulating expression of a gene by contacting the gene with a zinc finger protein which protein comprises a functional domain, wherein the functional domain cause repression or expression of the gene and the functional domain is a chromatin modulating domain. The claims of the instant application are drawn to a method for modulating expression of a gene by contacting the gene with a DNA binding domain (which is claimed in claims 6, 23, 31, 46, 54, 57, 58, 61, 63 and 67 as a zinc finger protein domain) and a chromatin remodeling complex (the chromatin modulating domain of copending Application No. 09/942,087 is claimed as a "DNMT" in claim 13, which is defined in copending Application No. 09/942,087 and in the instant application as a functional part of a chromatin remodeling complex). Claims 1-15 and 17-20 of copending Application No. 09/942,087 and

claims 1-6, 8, 10-13, 17-33 and 43-70 of the instant application are drawn to overlapping subject matter, and therefore, are obvious one over the other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

13. Arguments presented in Paper No. 16, filed April 11, 2003 assert that claims 1-15 and 17-20 of US Application Number 09/942,087 are directed to methods in which a component of a chromatin remodelling complex (DNMT) is used as a transcriptional regulator of gene expression. It is asserted that these limitations are distinct from the subject matter of instant claims 1-6, 8, 10-13, 17-33 and 43-70 which are drawn to methods in which a component of a chromatin remodelling complex is used in a first molecule to modify chromatin structure, not as a transcription regulator.

The instant claims are drawn to a method for modifying a region of interest in chromosomal cellular chromatin by contacting the chromosomal cellular chromatin with a fusion molecule comprising a DNA binding domain and a chromatin remodelling complex of functional fragment thereof. The above argument includes the term "structure" as a limitation of the claims. This limitation is not present in the instant claims. No limitation exists as to how the chromatin must be modified. Claims 1-15 and 17-20 of US Application Number 09/942,087 are drawn to a method of modulating expression of an endogenous cellular gene comprising contacting a target site in the endogenous cellular gene with a selected zinc finger protein. The protein also

comprises a functional domain. An endogenous cellular gene is a gene present in chromosomal cellular chromatin as required by the instant claims. The zinc finger has a DNA binding domain. Claim 13 of US Application Number 09/942,087 teaches that DNMT is the functional domain. DNMT modifies chromatin structure and is a component of a chromatin remodelling complex which is specifically listed in the instant specification at page 29, line 26. Therefore the limitations of instant claim 1 are met in the construction of a zinc finger protein comprising DNMT functional domain (which is a fusion protein comprising a DNA binding domain and a component of a chromatin remodelling complex). The method of US Application Number 09/942,087 claim 1 requires that the zinc finger/functional domain complex contacts the gene (chromosomal cellular chromatin) to modulate expression of the gene, thereby modifying the chromosomal cellular chromatin. Thus, the limitations of claims 1-15 and 17-20 of US Application Number 09/942,087 fulfill all of the requirements of instant claims 1-6, 8, 10-13, 17-33 and 43-70. The argument is therefore not found convincing and the rejection is sustained.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-6, 8, 10-13, 17-33 and 43-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1 and 43 recite "a component of a chromatin remodeling complex or functional fragment thereof". The claims and specification do not provide adequate written description of "a component of a chromatin remodeling complex or functional fragment thereof". Non-limiting examples of various species which may be "a chromatin remodeling complex" have been provided in the specification at page 2, line 20 bridging to page 5, line 6, and at page 6, and at page 24. However, no specific structural identifying features have been described for the genus of chromatin remodeling complexes. Further, no specific biological or chemical characteristics have been provided which describe "a **component** (emphasis added) of a chromatin remodeling complex or functional fragment thereof". No description has been provided to teach the skilled artisan what constitutes a "component" of a chromatin remodeling complex. Consequently, "a component of a chromatin remodeling complex or functional fragment thereof" may be nothing more than a hydrogen ion, which binds to, and thereby "modifies" a region of chromatin. This being the case, it is not possible to know the function of such an undefined "component". Consequently, a "functional fragment" is also not defined for the foregoing reasons. Thus, the phrase "a component of a chromatin remodeling complex or functional fragment thereof" is not supported by adequate written description for the term "a component of a chromatin remodeling complex or functional fragment thereof" in the instant claims and specification.

Response to Arguments

16. Arguments set forth in Paper No. 16, pages 5 and 6, assert that the claims do not encompass chromatin remodelling complexes that may be nothing more than a hydrogen ion. It is argued that the claims when properly construed will meet the limitations of "component of a chromatin remodelling complex" which is clearly described at page 23, line 24 through page 25, line 22 and also at pages 25-32. It is argued that abundant examples are given at these cited pages which provide an adequate description of the relevant identifying characteristics of the term "component of a chromatin remodelling complex" to provide evidence that the Applicant was in possession of the claimed invention.

The only teachings found at page 23 line 24 through page 25 line 22 which approach a definition of the term states "[t]wo major types of chromatin modification have been described. The first is dependent on covalent modification....The second type of modification results in changes in nucleosome location and/or conformation, and relies on the activity of ATP-driven chromatin remodelling machines. Both types of chromatin modification are carried out *in vivo* by multiprotein complexes. For the purposes of the present disclosure, proteins involved in either of these types of chromatin modification can comprise a component of a chromatin remodelling complex." The characteristics of a "component of a chromatin remodelling complex" are not set forth in this passage, nor at any other location in the specification. Further, since the term "comprising" is used in the above passage, it leaves open the question of what the identifying characteristics of a "component of a chromatin remodelling complex" may be.

At page 32, lines 19-26 a further elaboration of what is contemplated to be encompassed by the term "component of a chromatin remodelling complex" is set forth. Proteins as divergent as retinoblastoma protein (Rb) and other transcriptional regulatory proteins are said to be included in the meaning of the term. The broad reaching implications of this passage do not provide limitation, but rather invite an even wider meaning of the term. The relevant identifying and structural characteristics of the term "component of a chromatin remodelling complex" are therefore not set forth in the specification, but rather a collection of unrelated biological entities with unidentified limitations are described. The argument is therefore not found convincing.

17. It is argued in Paper No. 16, page 6 that the specification defines the term "functional fragment" at page 20, starting on line 21.

The passage which is recited refers to a definition of a functional fragment of a protein. The term "component of a chromatin remodelling complex" is not limited to functional fragments of a protein. Therefore, the cited definition only applies to that part of the constellation of "components of a chromatin remodelling complex" which may be proteins. Since the claims do not limit the term "component of a chromatin remodelling complex" to proteins, the argument is not found convincing.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 1-6, 8, 10-13, 17-33 and 43-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

20. Claims 1 and 43 recite the term "a component of a chromatin remodeling complex or functional fragment thereof". A "component of a chromatin remodeling complex or functional fragment thereof" is not defined in the specification or claims. Without proper guidance as to the meaning of the term, one of ordinary skill in the art would not know the metes and bounds of claims 1 and 43, and their dependent claims.

Response to Arguments

21. It is argued in Paper No. 16, page 7, that the term "component" is clearly defined on pages 23-35 of the specification, in particular page 23, line 24 to page 24, line 2. It is argued that the claim must be construed within the limits of the content of the disclosure, the teachings of the art and the interpretation given by one of ordinary skill in the art at the time the invention was made.

The cited passage concludes with "[f]or the purposes of the present disclosure, proteins involved in either of these types of chromatin modification can comprise a component of a chromatin remodelling complex." The relevant words which preclude this passage from being a definition are "can comprise". The open construction of these words precludes an ordinary skilled artisan from knowing the metes and bounds of the term "component of a chromatin remodeling complex or functional fragment thereof". The complex may have anything within

its meaning when the broadest interpretation of the claim language is made. The argument is therefore not found convincing, and the rejection is sustained.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

23. Claims 1-5, 8, 10, 12, 13, 17, 18 and 68-70 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,183,965 (Verdine et al.).

Verdine et al. teach at column 3, lines 1-21 a chimeric protein comprising a DNA-binding domain and a transcriptional modulator (component of chromatin remodelling complex). The chimeric protein binds to, and modifies a gene (erythropoietin) (region of cellular chromatin) (as recited in instant claims 1, 10, 12, 17, 18 and 68-70). At column 10, lines 28-63 the cell may be

in a plant, animal or human (as recited in instant claims 1-5). At column 21, line 5 to column 22, line 5 the chromatin remodelling complex may be an enzyme such as histone acetyl transferase (as recited in instant claim 8). The transcriptional modulator activates gene expression of a gene of interest , to facilitate detection of the gene of interest (as recited in instant claim 12). Alternatively, the transcriptional modulator may repress the expression of the gene of interest (as recited in instant claim 13). Erythropoietin is listed as a gene of interest at column 12, line 51 (as recited in claim 18). An exogenous molecule may be induced to bind to the complex (as recited in instant claims 10 and 68-70). The exogenous molecule may be a polypeptide, nucleic acid or a small molecule therapeutic (as recited in instant claim 18).

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. Claims 1-5, 8, 10, 12, 13, 17-22, 27-30, 43-45, 47, 51-53, 55, 56, 59 and 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,183,965 (Verdine et al.) in view of US 5,972,608 (Peterson et al.).

The claims are drawn to a method for modifying a region of interest in chromosomal cellular chromatin comprising contacting the chromosomal cellular chromatin with a fusion molecule that binds to a binding site in the region of interest. The fusion molecule comprises a DNA binding domain and a component of a chromatin remodelling complex. The cellular chromatin may be in a plant cell, an animal cell, which may be a human cell. The component of a chromatin remodelling complex may be an enzymatic component. Chromatin modification may facilitate detection of a gene of interest. The gene of interest may activated or repressed. The cellular chromatin may be contacted with a second molecule, which may be a transcriptional regulatory protein, or which may be a fusion polypeptide. There may be a third transcriptional regulatory protein, which may be a fusion polypeptide. The second molecule may be transcription factor, which may be either endogenous or exogenous. There may be a plurality of fusion molecules which modulate a plurality of genes. The modification of the chromatin may make a region of the chromatin accessible to binding an exogenous molecule. The exogenous molecule may be a polypeptide, nucleic acid, a small molecule therapeutic or major or minor groove binder.

Verdine et al. teach at column 3, lines 1-21 a chimeric protein comprising a DNA-binding domain and a transcriptional modulator (component of chromatin remodelling complex). The

chimeric protein binds to, and modifies a gene (region of cellular chromatin) (as recited in instant claim 1). At column 10, lines 28-63 the cell may be in a plant, animal or human (as recited in instant claims 1-5). At column 21, line 5 to column 22, line 5 the chromatin remodelling complex may be an enzyme (histone acetyl transferase) (as recited in instant claim 8). The transcriptional modulator activates gene expression of a gene of interest , to facilitate detection of the gene of interest (as recited in instant claim 12). Alternatively, the transcriptional modulator may repress the expression of the gene of interest (as recited in instant claim 13). Erythropoietin is listed as a gene of interest at column 12, line 51 (as recited in instant claims 17-18). An exogenous molecule may be induced to bind to the complex (as recited in instant claims 10 and 68-70). The exogenous molecule may be a polypeptide, nucleic acid or a small molecule therapeutic (as recited in instant claims 17-18). Verdine et al. teach at column 3 that there is at least one chimeric protein, suggesting more than one chimeric protein may be used in the method (as recited in instant claims 21-22, 29-30, 43-45, 47, 51-53, 55, 56 and 59).

The list of genes encoded by the gene of interest at claim 18 are listed in the instant specification as equivalents for the purposes of practicing the instant invention, one making the others obvious. Therefore, the teaching above in Verdine et al. of erythropoietin makes obvious the list of genes in claim 18.

Verdine et al. do not teach the use of two chromatin remodelling enzymes (proteins) to modify a chromosomal cellular chromatin.

Peterson et al. teach at the summary the use of two chromatin remodelling enzymes (proteins) to modify a chromosomal cellular chromatin (as recited in instant claims 43-67) which allows a direct comparison of the accessibility of chromosomal cellular chromatin by the chromatin remodelling enzymes.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the method of modifying chromosomal cellular chromatin with a fusion protein comprising a DNA binding domain and a component of a chromatin remodelling complex as taught by Verdine et al. with the two protein method of modifying chromatin as taught by Peterson et al. since Verdine et al. clearly suggest using more than one chromatin remodelling complex. One of ordinary skill in the art would have been motivated to combine the teachings of Peterson et al. with Verdine et al. for the expected benefit of making a direct comparison of the accessibility of the chromosomal cellular chromatin by the component of a chromosomal remodelling complex. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Verdine et al. who demonstrate a method of modifying cellular chromatin with a component of a cellular remodelling complex and Peterson et al. who demonstrate the use of two enzymes for remodelling cellular chromatin.

27. Claims 1-6, 8, 10, 12, 13, 17-33 and 43-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,183,965 (Verdine et al.) in view of US 5,972,608 (Peterson et al.) as

applied to claims 1-5, 8, 10, 12, 13, 17-22, 27-30, 43-45, 47, 51-53, 55, 56, 59 and 68-70 above, and further in view of Cardoso et al. and Omichinski et al.

The claims are drawn to the invention as described above and where the DNA binding protein is a zinc finger DNA binding domain.

Verdine et al. and Peterson et al. teach the invention as described above.

Verdine et al. and Peterson et al. do not teach that the DNA binding protein is a zinc finger DNA binding domain.

Cardoso et al. teach at the abstract and at page 683, column 1, a zinc finger DNA binding domain protein in a fusion protein used in a method of modifying a region of cellular chromosomal chromatin (as recited in instant claims 23-26, 31-33, 46, 48-50, 54, 57-58, 61, 63 and 67). The fusion protein comprises a component of a chromatin remodelling complex which is used in a method of expression of a gene of interest.

Omichinski et al. teach at page 130 (Relationships to Chromatin Remodelling) a zinc finger DNA binding domain in a fusion protein where the fusion protein is used in a method of chromatin remodelling and control of expression of a desired gene. The protein binds to DNA in the major and minor groove of the target DNA to facilitate access to chromatin in a method of chromatin remodelling (as recited in instant claims 21-26, 31-33, 46, 48-50, 54, 57-58, 61, 63 and 67-70).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combining the method of modifying chromosomal cellular chromatin with

a fusion protein comprising a DNA binding domain and a component of a chromatin remodelling complex as taught by Verdine et al. and Peterson et al. with the zinc finger DNA binding protein which is used in a method of modifying (remodelling) chromatin as taught by Cardoso et al. and Omichinski et al. One of ordinary skill in the art would have been motivated to combine the teachings of Peterson et al., Verdine et al., Cardoso et al. and Omichinski et al. for the expected benefit of facilitating access to chromatin for expression of a desired gene in a method of chromatin remodelling. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Verdine et al. who demonstrate a method of modifying cellular chromatin with a component of a cellular remodelling complex, Peterson et al. who demonstrate the use of two enzymes for remodelling cellular chromatin, Omichinski et al. who demonstrate a method of chromatin remodelling using a zinc finger DNA binding domain and Cardoso et al. who also demonstrate a method of chromatin remodelling using a zinc finger DNA binding domain.

28. Claims 1-6, 8, 10-13, 17-33 and 43-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,183,965 (Verdine et al.) in view of US 5,972,608 (Peterson et al.) and further in view of Cardoso et al. and Omichinski et al. as applied to claims 1-6, 8, 10, 12, 13, 17-33 and 43-70 above, and further in view of Rutter et al.

The claims are drawn to the invention as described above and where the sequence of interest comprises a single nucleotide polymorphism.

Verdine et al., Peterson et al., Cardoso et al. and Omichinski et al. teach the invention as described above.

Verdine et al., Peterson et al., Cardoso et al. and Omichinski et al. do not teach that the sequence of interest comprises a single nucleotide polymorphism.

Rutter et al. teach at the abstract and discussion, a change in transcriptional control of expression of a gene with a single nucleotide polymorphism in the gene promoter region. The single nucleotide polymorphism directly changes the accessibility of the DNA by a DNA binding protein as a result of chromatin remodelling by a component of a chromatin remodelling complex (as recited in instant claim 11).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the method of modifying chromosomal cellular chromatin with a fusion protein comprising a DNA binding domain (zinc finger protein) and a component of a chromatin remodelling complex as taught by Verdine et al., Peterson et al., Cardoso et al. and Omichinski et al. with the gene which has a single nucleotide polymorphism and increases the accessibility of the gene to DNA binding protein as a result of chromatin remodelling by a component of a chromatin remodelling complex as taught by Rutter et al. One of ordinary skill in the art would have been motivated to combine the teachings of Peterson et al., Verdine et al., Cardoso et al., Omichinski et al. and Rutter et al. for the expected benefit of increasing access to chromatin by the DNA binding protein (zinc finger protein) in a method of control of gene expression by chromatin remodelling. Further, a person of ordinary skill in the art would have

had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Verdine et al. who demonstrate a method of modifying cellular chromatin with a component of a cellular remodelling complex, Peterson et al. who demonstrate the use of two enzymes for remodelling cellular chromatin, Omichinski et al. who demonstrate a method of chromatin remodelling using a zinc finger DNA binding domain, Cardoso et al. who also demonstrate a method of chromatin remodelling using a zinc finger DNA binding domain and Rutter et al. who demonstrate that a single nucleotide polymorphism can alter the effect of a component of a chromatin remodelling complex on the expression of a desired gene

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Conclusion

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.
Examiner
June 14, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600